

anticonvulsant effect of the ketogenic diet was unrelated to diuresis, independent of acidosis and ketosis, similar to the effects of acetazolamide, and correlated most closely with a negative balance of sodium and potassium.

## ANTICONVULSANT SIDE EFFECTS

### **COGNITIVE EFFECTS OF PHENOBARBITAL**

Neurocognitive behavior in 9 children with various epilepsies was evaluated before and at 6 months after discontinuing phenobarbital monotherapy at the Department of Child Neurology, Istituto Nazionale Neurologico "Carlo Besta," Milano, Italy. The patients had been seizure-free for at least 2 years. All of the scores on the WISC improved and the mean Performance IQ was significantly higher after phenobarbital was withdrawn. Other tests showing significant improvement included the general information subtest on the Verbal IQ, picture arrangement on the Performance IQ, visual spatial memory, and visual-motoric and attentional skills, as measured by coding and the Trail Making test. (Riva D, Devoti M. Discontinuation of phenobarbital in children: Effects on neurocognitive behavior. Pediatr Neurol 1996;14:36-60). (Respond: Dr Riva, Department of Child Neurology, Istituto Neurologico "Carlo Besta;" 11 Via Celorio, 20133 Milano, Italy).

COMMENT. In this small number of children treated, phenobarbital appeared to have impaired attention, spatial memory, and visual/motor skills. The deficits were reversible and disappeared when phenobarbital was discontinued.

**Drowsiness secondary to chronic antiepileptic drug therapy** was assessed in 30 patients, using an EEG-based Awake Maintenance Task (AMT) measure, and reported from the Portland Veterans Affairs Medical Center, and Oregon Health Sciences University, Portland, Oregon. (Salinsky MC et al. Epilepsia 1996;37:181-187). Ability to maintain wakefulness was determined during a 6-min unstimulated trial. One third of AED-treated patients had >120 s of drowsiness in contrast to only 1 of 63 controls. Objective EEG drowsiness did not correlate with AED levels or performance measures. Untreated seizure patients had more complaints of lack of vigor despite absence of objective drowsiness on the AMT. Subjective reports of AED-related drowsiness may be unreliable.

### **LAMOTRIGINE-INDUCED SKIN RASH**

Five of 68 consecutive children treated for epilepsy with lamotrigine developed a skin rash, one a Stevens-Johnson syndrome, in a report from Dalhousie University, and IWK Children's Hospital, Halifax, Nova Scotia, Canada. Two patients required intensive care. The interval between introduction of lamotrigine and the rash varied from 2 to 8 weeks. One child in whom the drug was reintroduced after 6 months had a recurrence of the rash within 30 minutes of a single small dose. In 4 patients taking concomitant therapy, the AEDs were continued during and after the lamotrigine-induced rash. (Dooley J, Camfield P et al. Lamotrigine-induced rash in children. Neurology Jan 1996;46:240-242). (Respond: Dr Joseph M Dooley, Neurology Division, IWK Children's Hospital, 5850 University Avenue, Halifax, Nova Scotia, Canada B3J 3G9).

COMMENT. Skin rash, especially Stevens-Johnson syndrome, is one of the most disturbing side-effects of AEDs. The introduction of any

anticonvulsant, especially carbamazepine, should be accompanied by a parental warning of possible skin rash, particularly during the first 2 weeks of treatment. In my own view, a drug having once caused a serious skin rash should never be readministered to the sensitive individual. For reviews of carbamazepine-induced skin rash, including use of prednisone in treatment, see Progress in Pediatric Neurology II, PNB Publ, 1994, pp 107-109.

## HEPATIC FATALITIES AND VALPROIC ACID

The results of a third retrospective study of the US experience since 1986 with fatal hepatotoxicity associated with valproic acid (VPA) are reported from the Department of Neurology, University of Virginia School of Medicine, Charlottesville, VA. In 29 case fatalities, the most common presenting signs were drowsiness, jaundice, vomiting, hemorrhage, seizure exacerbation, anorexia, and edema. Risk factors included young age, especially below 2 years when the risk was 1:600, polytherapy, developmental delay, and coincident metabolic disorders, especially Alpers' disease. (Bryant AE III, Dreifuss FE. Valproic acid hepatic fatalities. III. US experience since 1986. Neurology Feb 1996;46:465-469). (Reprints: Dr Fritz E Dreifuss, Department of Neurology, Box 394, University of Virginia Health Sciences Center, Charlottesville, VA 22908).

COMMENT. The authors advise avoidance of VPA in patients who are at greatest risk of developing liver toxicity. Liver transplant had been received by 28% of the patients in this study.

## CHOREOATHETOSIS WITH GABAPENTIN

A 37-year-old man with severe mental retardation since birth and intractable epilepsy treated with AED polytherapy developed choreoathetosis and orofacial dyskinesia within 5 days of introducing gabapentin (GBP) at the Department of Neurology, West Virginia University, Morgantown, WV. Diphenhydramine 25 mg IV resulted in improvement and movements resolved within 2 days of discontinuing GBP. Other AEDs were continued and dosages were unchanged. (Bueteifisch CM et al. Choreoathetotic movements: a possible side effect of gabapentin. Neurology March 1996;46:851-852). (Reprints: Dr Catherin M Bueteifisch, Department of Neurology, Robert C Byrd Health Sciences Center, West Virginia University, Morgantown, WV 26506).

COMMENT. AED-induced movement disorder is rare, but is described with phenytoin, carbamazepine, ethosuximide, and with felbamate. This is the first reported case with gabapentin.

**Exacerbation of seizures in Lennox-Gastaut syndrome by gabapentin** is described in a 14-year old boy from the Epilepsy Center, Swedish Medical Center, Seattle, WA. (Vossler DG. Neurology March 1996;46:852). Gabapentin (GBP), 300 - 600 mg tid, was added to valproate and methsuximide therapy, and absence and myoclonic seizures were markedly exacerbated. A generalized tonic-clonic seizure also occurred for the first time since undergoing corpus callosotomy at age 9 years. When GPA was discontinued over 4 days and phenytoin was added, no seizures recurred in the subsequent 7 months follow-up.